PLATEFORME REGIONALE DE RECHERCHE CLINIQUE THA
TRYPANOSOMIASE HUMAINE AFRICAINE
HUMAN AFRICAN TRYPANOSOMIASIS
HAT REGIONAL PLATFORM FOR CLINICAL RESEARCH

HAT

REGIONAL PLATFORM FOR CLINICAL RESEARCH

Platform

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PARTICIPATION OF THE HAT PLATFORM IN THE 36TH GENERAL CONFERENCE OF THE INTERNATIONAL SCIENTIFIC COUNCIL ON TRYPANOSOMIASIS RESEARCH AND CONTROL

MOMBASA, KENYA, 18-22 SEPTEMBER 2023

Partenaires

International and national research groups : CDC, TRC-KARI

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EDITORIAL

Dear Reader,

This 23rd HAT Platform Newsletter is a special edition focusing on the Platform's participation in the 36th conference of the International Scientific Council for Trypanosomiasis Research and Control (ISCTRC), held from 18 to 22 September 2023 in Mombasa, Kenya.

In this issue, we announce that the European Medicines Agency (EMA) has issued a positive opinion for fexinidazole, the first oral drug for the treatment of *rhodesiense* human African trypanosomiasis (r-HAT) and WHO published treatment guidelines. This is good news for affected populations in the endemic countries of East Africa. WHO has aslo recognised Chad as the first country to have eliminated sleeping sickness by 2024, becoming the 51st country to achieve this goal in the world, and congratulates Chad's goverment and the people of Chad on this achievement. We also discuss the HAT Platform Steering Committee meeting, the progress of fexinidazole access activities and the StrogHAT project on the treatment of g-HAT seropositive suspects in the DRC using the Screen & Treat strategy with single-dose acoziborole.

In all our newsletters, we remind you that the integrated control of neglected tropical diseases (NTDs) is an approach supported by the WHO, and that it must be a focus of research. Given this, we present here the research projects currently underway on onchocerciasis, as well as programmes to provide access to antiretroviral treatment for children living with HIV in the DRC, who are also neglected patients.

Happy reading to all.

Dr. Florent Mbo Kuikumbi

HAT PLATFORM PARTICIPATION IN THE 36TH CONFERENCE OF THE INTERNATIONAL SCIENTIFIC COUNCIL FOR TRYPANOSOMIASIS RESEARCH AND CONTROL (ISCTRC), 18-22 SEPTEMBER 2023, MOMBASA, KENYA

By Albert Nyembo, Alphonsine Bilonda and Florent Mbo

The HAT Platform financially supported the participation of its members and other scientists whose abstracts had been accepted. The HAT Platform participating members came from Angola (2 people), CAR (2), Chad (2), DRC (21), Guinea (6), Malawi (1), South Sudan (3) and Uganda (2).

The highlight of this conference for the HAT Platform was the participation of its members and guests in the HAT session on 20 September 2023. The 19 oral presentations were divided into five themes: diagnosis, screening and elimination strategies, treatment and vaccines, animal reservoirs and vector control for HAT elimination and African animal trypanosomiasis.

A. Summary of two HAT session oral presentations

1. Geo-spatial monitoring: a targeted and integrated approach to accelerate HAT elimination in the Republic of Guinea

By Moise Kagbadouno et al.

The objective of HAT elimination as a public health problem was achieved through a combination of medical control and vector control introduced in Guinea in 2012. To build on these achievements, the national programme put in place a targeted strategy, tailored to the hypo-endemic context, to accelerate the transmission interruption process. This strategy includes four stages:

- In-depth epidemiological questionnaire of screened patients
- Geo-spatial monitoring around these patients to identify areas at risk
- Entomological survey in the identified areas
- Targeted reactive control measures with deployment of insecticide-impregnated tiny targets and door-to-door screening in the identified areas.

Between October 2022 and February 2023, eight patients screened at the Dubréka centre were followed up. Nine areas were identified as these patients' workplaces, located in fishing grounds, salt farming and rice fields, a third of which were not covered by vector control measures. A total of 74 tsetse flies were captured and 50 tiny targets deployed. At the end of March 2023, a door-to-door screening campaign targeting 947 people in those areas identified five HAT cases. These results show that geo-spatial monitoring is able to identify cases that would otherwise have gone unnoticed. The effectiveness of this approach relies on close cooperation between medical and entomological control activities.

2. Active HAT screening in non-endemic villages by a Bagata health zone team in the DRC

By Matthieu Nkieri et al.

Despite a declining prevalence of HAT, there is still a risk of re-emergence of cases in the DRC because of the precariousness of the health system and the geographical location of former HAT foci in endemic health zones poorly covered by the surveillance system. Following the success of active screening to detect cases in former HAT foci in Côte d'Ivoire, Gabon[1] and Guinea, the same experience was repeated in the Bagata health zone.

The aim of this study was to document the epidemiological status of HAT in the former foci of the Bagata health zone, through active screening in villages 'extinct' for more than ten years. The Bagata health zone covers 7,000 km^2 with a total population of 223,667 (2023), and it has an operational mobile team from the NSSCP.

Data was collected in 19 non-endemic villages, of which nine were visited, and 7,310 people were examined out of a registered population of 8,620. A total of 67 CATT positive serological suspects were identified, and a mini-column anion-exchange test (mAECT) was run for 51 of them, which confirmed seven new cases (three stage 1 and four stage 2).

In conclusion, in a context of declining prevalence, HAT elimination in endemic health zones or districts requires a combination of current strategies (active and passive screening, treatment of patients and vector control), with the integration of control activities into the annual operational plan, as well as active case-finding in the endemic health zone in former HAT foci that had been declared extinct.

B. Recommendations to the HAT session participants

This session was chaired by the Coordinator of the HAT Platform, assisted by the Platform's focal point in Uganda as rapporteur.

The session was opened by the World Health Organisation (WHO) with a recap on HAT epidemiology from 1940 to 2022, leading to a drastic decline in the number of cases worldwide to below the elimination threshold. As a result, HAT is no longer considered a public health problem in most endemic countries, seven of which have formalised this position: Benin, Côte d'Ivoire, Equatorial Guinea, Ghana, Togo and Uganda for *T.b. gambiense* HAT (g-HAT), and Rwanda for *T.b. rhodesiense* HAT (r-HAT).

The objective set out in the WHO roadmap is to interrupt g-HAT transmission and eliminate r-HAT as a public health problem by 2030. As a zoonosis, r-HAT must be tackled as part of the 'One Health' approach. The drugs currently used on the ground to treat this *T.b. rhodesiense* form of the disease are highly toxic, and the development of serological tests, which are currently non-existent, would enable initial screening to be carried out before microscopy. In December 2023, EMA has issued a positive opinion for fexinidazole for r-HAT. New opportunities will be provided by new diagnostics, the development of new drugs (acoziborole), social science research to improve active screening and referral of samples to reference laboratories, affordable and easy-to-use vector control tools and various WHO technical advisory committees.

1 Kohagne TL, M'eyi MP, Kamkuimo RG, Kaba D, Louis JF, Mimpfoundi R. Transmission of human African trypanosomiasis in the Komo-Mondah focus, Gabon. Pan Afr Med J. 2011;8:36. doi: 10.4314/pamj.v8i1.71151. Epub 2011 Apr 1. PMID: 22121444; PMCID: PMC3201599.

1. HAT diagnosis

a. Given the variability of RDT results used in different settings. It is so important to improve the tests' performance, and particularly their specificity, to ensure compliance with WHO Target Product Profile (TPP) characteristics, and thus reduce false positives. The availability of CATT must be guaranteed, as it is currently the test of choice for active screening.

1 Kohagne TL, M'eyi MP, Kamkuimo RG, Kaba D, Louis JF, Mimpfoundi R. Transmission of human African trypanosomiasis in the Komo-Mondah focus, Gabon. Pan Afr Med J. 2011;8:36. doi: 10.4314/pamj.v8i1.71151. Epub 2011 Apr 1. PMID: 22121444; PMCID: PMC3201599.

b. The correlation between molecular and serological reference tests must be improved, with further research on and evaluation of the performance of existing tests and tests under development.

c. The development of serological tests such as RDTs for r-HAT will greatly improve the detection of this form of the disease. Research in this area is strongly encouraged.

2. HAT screening and elimination strategies

a. HAT elimination activities primarily target known endemic foci, but knowledge of historical/silent foci needs to be improved and surveillance methods adapted.

b. Current challenges in active screening (e.g., decreasing community participation) and passive screening (e.g., integration in weak peripheral health systems) should be taken into account when proposing new, adapted and innovative approaches. It is also important to take into account socio-cultural aspects to encourage community participation in active screening.

c. Known additional actions, such as participation in screening activities, should be included in models to address local issues.

d. Cost-effectiveness modelling studies can be useful to guide control interventions aiming for HAT elimination in endemic countries.

3. HAT treatments

a. In view of the results of fexinidazole clinical studies in r-HAT, WHO support for the regulatory application for this new fexinidazole indication is recommended. In g-HAT endemic countries, more than 60% of reported r-HAT cases are already treated with fexinidazole.

b. The indications of newly developed drugs do not adequately target children, pregnant and breast-feeding women, or g-HAT seropositive suspects. Consequently, clinical research on new drugs (e.g., acoziborole) should be extended to these population groups.

4. Animal reservoirs and vector control in HAT elimination

a. Further studies are needed to improve our understanding of the role played by animal reservoirs in g-HAT transmission.

b. Vector control must be combined with other HAT elimination strategies. One Health studies have shown a positive impact and need to be broadened.

5. Animal African trypanosomiasis (AAT)

a. AAT research and control activities must be integrated in collaboration with veterinary services.

b. A robust database/information system (e.g., atlas) should be developed for tsetse and TAA to guide evidence-based decision making.

c. Research into new trypanocides effective against all trypanosomes should be accelerated.

d. Laboratory capacities and diagnostics for TAA must be strengthened, potentially with the support of the World Organisation for Animal Health (WOAH) through its Laboratory Twinning Programme to train laboratory staff.

e. Regional reference laboratories for AAT diagnosis should be established on the African continent and recognised as WOAH Collaborating Centres.

Delegates of the ISCTRC conference held in Mombasa on 18-22 September 2023 stress the importance of trypanosomiasis and its impact on human health and animal productivity, particularly in sub-Saharan Africa. They praise the major advances made in HAT control, thanks to the commitment of many actors and numerous initiatives to control the disease and its vector, tsetse flies. HAT is no longer a public health problem in some countries and is in the process of ceasing to be one in others. In addition, many animal health actors are mobilised to eliminate tsetse flies and mechanical vectors. The delegates are grateful to the African Union's Interafrican Bureau for Animal Resources (AU-IBAR) for their mobilisation of resources to foster coordinated action against African trypanosomiasis in association with the ISCTRC.

Opening speech of the African Union representative

They note the significant role and contribution of this forum, which brings together several tsetse and trypanosomiasis control actors.

They point out that seven Member States of the African Union have eliminated HAT as a public health problem, and that several other countries have adopted the same progressive control process (PCP) against African animal trypanosomiasis (AAT).

They recognise that past and current trends point to increasingly severe, recurrent and often more widespread complex crises, exacerbated by re-emerging threats, and that significant investment, policy, regulatory and institutional reforms are needed.

Recommendations formulated at the conference:

a. The FAO (Food and Agriculture Organization) and AU should continue to promote the rationalisation of the Progressive Control Process (PCP) in national and regional policies and strategies for the control of African animal trypanosomiasis.

b. The International Atomic Energy Agency (IAEA) and AU should strengthen capacity

building in Member States for informed decision-making on the choice of tsetse and trypanosomiasis control strategies, and the cost-effective integration of sterile insect technique (SIT) interventions into integrated pest management in all endemic foci, with the aim of creating and expanding tsetse-free zones.

c. They call on all stakeholders to mobilise their concerted efforts to re-launch the PATTEC (African Tsetse and Trypansomiasis Eradication Campaign) initiative for effective tsetse and trypanosomiasis control and elimination in Africa. This should be included on the agenda of the next AU Summit.

d. The AU should renew its efforts to reactivate functions to provide coordination and leadership for the continent.

e. PATTEC should be reactivated as an institution collaborating with WAHO.

f. Cross-border projects should be developed for the research and control of HAT, AAT and vectors.

g. Financial support should be provided to regional insectariums in Burkina Faso and Ethiopia for mass production of sterile tsetse flies so that PATTEC countries can deploy the SIT.

Opening ceremony by Deputy President of Kenya (3rd from the left)

REPORT OF THE REGIONAL HAT PLATFORM STEERING COMMITTEE, 16 SEPTEMBER 2023, MOMBASA, KENYA

By Albert Nyembo, Alphonsine Bilonda and Florent Mbo

HAT platform steering committee meeting

The meeting was held in conjunction with the 36th ISCTRC General Conference in Mombasa, Kenya. It was chaired by the Coordinator of Guinea's Neglected Tropical Diseases Programme, assisted by a representative of the DRC, a representative of Uganda and the Coordinator of the HAT Platform.

A minute's silence was observed in memory of Dr Peka Mallaye, Chad's HAT Platform Coordinator, and the other deceased members. The member countries present at the meeting included Angola, CAR, Chad, DRC, Guinea, South Sudan, Sudan and Uganda. Malawi participated as an observer. The HAT Platform Coordinator provided an update on the Platform's activities in 2022 and the first half of 2023, with an outlook for 2024. One of the concrete achievements was the use of fexinidazole, the new oral treatment for both stages of sleeping sickness, in all g-HAT endemic countries thanks to a collaboration with the WHO and other partners.

Other activities included participation of HAT Platform members and researchers in the 36th ISCTRC General Conference, supporting pharmacovigilance activities in the five countries most endemic for g-HAT (Angola, CAR, DRC, Guinea and South Sudan), and the publication of the 22nd HAT Platform Newsletter in February 2023.

Activities planned for Q4 2023 and 2024 include organising the FEX-g-HAT project management committee and advisory board meeting, pharmacovigilance guideline validation activities, training on HAT electronic reporting and diagnosis in CAR and South Sudan and organising the 6th joint HAT Platform-EANETT scientific meeting.

The countries presented research projects involving various HAT Platform partners.

The WHO representative focused his presentation on the organisation's role in HAT research, strategies and guidelines, research support and updates of new treatments tested for g-HAT and r-HAT. As regards pharmacovigilance with the post-authorisation safety study, ten countries have already reported around 500 treated cases and sent in adverse event report forms. This study will continue until December 2024. He also pointed out that seven countries have formalised their elimination of HAT: Benin, Côte d'Ivoire, Equatorial Guinea, Ghana, Rwanda, Togo and Uganda. Since then, Chad announced its elimination in June 2024: https://www.who.int/fr/news/item/20-06-2024-chad-eliminates-human-african-trypanosomiasis-as-a-public-health-problem

PROJETS	COUNTRIES	PARTNERS
TrypaNO 3	Chad, Ivory Coast, Guinea and Uganda	FIND, IRD-Cirad Intertryp, LSTM, Vestergaard, CIRDES, Guinea and Chad NSSCP, IRED, COCTU. Steering Committee of Côte d'Ivoire: IRD, PNLTHA, IPR Bouaké, UJLoG Daloa
Trypskin	DRC and Guinea	Institut Pasteur, DNDi, Guinea and DRC NSSCP, INRB, IMT, IRD
Clinical trial on acoziborole (OXA004) in seropositive adults	DRC and Guinea	DNDi, IRD
Clinical trial on acoziborole (OXA005) in seropositive children	DRC and Guinea	DNDi, IRD
StrogHAT Project (Screen & Treat approach with acoziborole)	DRC	IMT, INRB, DRC NSSCP, IRD, DNDi
HAT-r-ACC Consortium	Malawi and Uganda	DNDi, Ministry of Health (Malawi), UNHRO (Uganda), University of Makerere (Uganda), Epicentre, IRD, Swiss TPH, IMTH of Lisbon
Modelling and evaluation of control strategies	DRC	University of Warwick, Swiss TPH

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ACTIVITIES OF THE FEXINIDAZOLE ACCESS PROJECT FOR G-HAT, SUPPORTED BY DNDI AND ITS PARTNERS, AND IMPLEMENTED BY THE HAT PLATFORM

By Albert Nyembo, Alphonsine Bilonda and Florent Mbo

This project focuses on HAT diagnosis and access to fexinidazole in populations aware of and affected by the disease, to support the WHO's HAT elimination objective.

The activities include capacity building (diagnosis, treatment, search for serological suspects, supervision, rehabilitation, equipment and communication), public access to the new drug (fexinidazole), and supporting the health systems of member countries for integration, pharmacovigilance and community awareness.

The countries' results from the start of this access project in 2019 up to 2023 are summarised in the table below.

ACHIEVED	COUNTRIES
Training on the use of fexinidazole in line with the new WHO guidelines	Angola, Burkina Faso, Cameroon, CAR, Congo, DRC, Equatorial Guinea, Gabon, Guinea, South Sudan, Chad and Uganda
Training on screening with rapid diagnostic tests (RDT)	DRC
Adoption or adaptation of the new WHO guidelines on g-HAT treatment	DRC, Angola, Burkina Faso, Cameroun, Congo, Gabon, Guinée, Guinée équatoriale, Ouganda, RCA, Soudan du Sud et Tchad,
Educational materials on g-HAT and r-HAT produced and distributed during the training of opinion leaders	DRC, Malawi and Uganda
Rehabilitation and equipping of health centres to improve HAT-related services	DRC
Creation of a reference and confirmation network for serological suspects identified by passive screening, with blood samples sent for trypanolysis to the INRB national reference laboratory.	DRC
Electronic reporting of adverse events via the national pharmacovigilance system	CAR, DRC and Guinea
Ethnographic study of the perceptions and beliefs about g-HAT of people living in endemic areas	DRC

Support for the adoption of pharmacovigilance guidelines	CAR and Guinea
Strategy for screening and treatment with acoziborole (serological suspects and children)	DRC
Reactive active screening for HAT	CAR, South Sudan
Training of national pharmacovigilance systems	Angola, CAR, DRC, Guinea and South Sudan
Training of laboratory technicians to diagnose HAT using sensitive parasitological tests (mini-column)	CAR, Guinea and South Sudan
Organisation of workshops to validate pharmacovigilance guidelines and delivery of IT equipment	CAR, DRC, Guinea and South Sudan
Training of national pharmacovigilance systems in electronic reporting	CAR, DRC, Guinea and South Sudan
Start of electronic reporting of adverse events via the national pharmacovigilance system	Angola and South Sudan
Use of Vigiflow software to report adverse events to the Uppsala Monitoring Centre	Angola, CAR and DRC
Online training for country pharmacovigilance focal points at the Moroccan Poison and Pharmacovigilance Centre	Angola, CAR, DRC and Guinea

ACTIVITIES IN PROGRESS OR PLANNED FOR 2024	COUNTRY
Training of pharmacovigilance team in electronic reporting	Angola
Reactivation of Vigiflow software for reporting of adverse events at the Uppsala Centre	Guinea, South Sudan


Burkina Faso, 21-22 January 2022


South Sudan, 8-11 November 2021

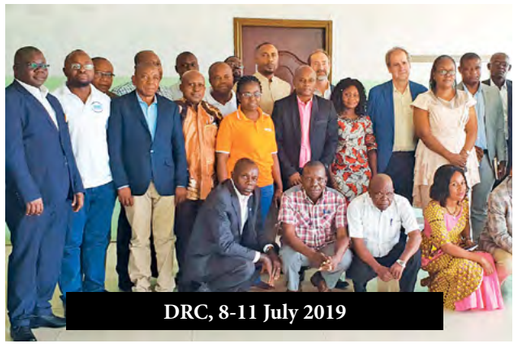

Guinea, 21-22 January 2022


CAR, 24-31 August 2021


Cameroon, 29 November - 1 December 2021


Guinea, 20-24 January 2022


Uganda, 4 April 2022.


DRC, 8-11 July 2019

OVERVIEW OF THE STROGHAT PROJECT LED BY THE INSTITUTE OF TROPICAL MEDICINE ANTWERP, BELGIUM

By Elena Nicco

STROGHAT Study investigators' meeting

The StrogHAT epidemiological study is designed to assess the impact of acoziborole treatment in g-HAT seropositive suspects on parasite transmission, and to collect additional safety data in this population. This clinical study is being conducted by five partners, including the NSSCP and INRB in the DRC, as well as international partners such as DNDi, IRD and ITM.

The primary study coordinator, ITM, is responsible for the epidemiological component. DNDi is the legal sponsor of the safety clinical study and, as such, will ensure compliance with regulatory requirements and good clinical practice (GCP). The NSSCP is in charge of controlling implementation activities, while INRB is responsible for diagnosis with the support of IRD.

The study is part of a five-year project funded by the European Union through Horizon Europe (HORIZON-JU-GH-EDCTP3-2022-01- Project: 101103189) and draws upon decades of g-HAT control activities performed in the DRC by the NSSCP, with the support of WHO and partners.

Over the past decades, g-HAT has caused hundreds of thousands of deaths in the DRC, with a peak in the late 1990s. Thanks to sustained local and global efforts, the disease is once again under control, but new strategies must be implemented to keep it under control permanently. Acoziborole is a non-toxic single-dose oral drug effective against both stages of g-HAT, which could be used to treat anyone with a positive serological screening test, without further need for on-site parasitological confirmation and stage determination.

This will greatly simplify procedures in the field, may increase screening uptake by affected populations, and will widen the treatment to all g-HAT seropositive suspects, thereby reducing the number of undetected cases. This could open up new possibilities of eliminating the disease, assuming no animal reservoirs play a major role in g-HAT transmission.

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The objective of the StrogHAT study is to determine whether zero g-HAT prevalence can be achieved over a three-year period when implementing a Screen & Treat approach using acoziborole in a g-HAT focus in the north-west of the DRC.

As acoziborole is not yet registered, and the Screen & Treat approach has not yet been adopted, we will continue to perform on-site parasitological confirmation and treat anyone with positive parasitology with the standard of care for the duration of this study. Any serological suspect not confirmed by on-site parasitology will be asked to provide informed consent and offered treatment with acoziborole, conditional on inclusion and exclusion criteria.

The clinical study aims at generating further evidence on the safety of acoziborole in serological g-HAT suspects currently included in an ongoing phase II/III safety study. Although the results of treatment in confirmed g-HAT cases have shown a favourable risk-benefit profile so far, a detailed assessment of a greater number of cases is imperative before adopting a large-scale Screen & Treat approach.

We will also evaluate the cost of the Screen & Treat approach, which will be a key parameter in the decision to roll it out on a large scale, and we will evaluate the specificity and positive predictive value of the screening tests used in the field and in reference laboratories.

The study will take place in the DRC's endemic provinces of North Ubangi, South Ubangi and Mongala. During the study period, g-HAT seropositive suspects will be identified through active and passive screening activities already underway in the region. Three NSSCP mobile units, one mobile mini-unit and 30 fixed Ministry of Health facilities, including five main study sites, will take part in the study.

The provincial NSSCP coordination will coordinate activities at a local level, together with partners, local actors and the authorities. Over the past months, an acceptability study was conducted to assess factors that might foster community participation in g-HAT screening and treatment in the study area, this will help focus the implementation of the StrogHAT study as well as related activities promoting communication and awareness. For further information on the StrogHAT study, click on this link: https://www.itg.be/en/research/projects/stop-transmission-of-gambiense-human-african-trypanosomiasis-stroghat.

Training on Communications tools for the STROGHAT study

LESSONS LEARNED FROM G-HAT MODELLING IN 2023 BY THE UNIVERSITY OF WARWICK

By Katerine Rock

Our team leading the Human African Trypanosomiasis Modelling and Economic Predictions for Policy (HAT MEPP) project kicked off the year 2023 with a focus on modelling for the DRC and participating in the DRC HAT day in Kinshasa.

We concentrated on key methodological developments, including capacity building to fit the model to the smaller spatial scale of health zones (Davis et al., *MedRxiv*, 2023), and the use of data trends to assess the potential impact of asymptomatic skin infections on transmission (Aliee et al., in prep). The results demonstrated moderate statistical support for asymptomatic transmission in the DRC, but also a seemingly low risk of interference from asymptomatic infections in HAT elimination. A more pressing issue will be to deploy proven field tools in appropriate regions.

Our latest health economic evaluation in the DRC showed that many health zones are expected to reach elimination by 2030 if their current strategy remains unchanged (Antillon et al., in prep). Moreover, elimination is predicted to be epidemiologically feasible in most other regions with currently available tools, provided needs in terms of funding, training and personnel are met. This is particularly relevant for the regions in the east of the DRC.

As modelling suggests that operationalisation will be one of the HAT community's biggest challenges, one of our priorities for 2024 will be to improve small-scale forecasting of tool use to support the national programme, particularly for drug treatment and screening tests. This work will also include a scenario where acoziborole could be used in Screen & Treat approaches.

The HAT MEPP team has also been working collaboratively with the national sleeping sickness teams and their supporting partners from Chad, Côte d'Ivoire, Guinea and Uganda to assess and support their progress towards elimination. We caught up with many of them during the WHO Stakeholders meeting in Geneva and the ISCTRC conference in Mombasa, during which they highlighted their recent successes and adaptive approaches to tackling remaining cases.

This progress is based on advances provided by our team, such as coupling case data with our transmission model to demonstrate that intensified interventions in the Mandoul focus of Chad were a cost-effective use of resources (Antillon et al., 2023). Ongoing modelling for each country involves a quantitative evaluation of past HAT transmission and the likely impact and associated costs of planned or possible future strategies. The HAT MEPP team ended 2023 with a visit to Guinea, where it experienced first-hand the national programme's challenges in collecting data and planning interventions when case reporting is very low and targeted populations are hard to reach.

Our visit ended with a modelling workshop highlighting the importance of data and its interpretation to generating robust models, the types of questions modelling can and cannot answer, and the importance of detailed discussions between the modellers and the national programmes to create meaningful results. Updates will be published in 2024.

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SPESERTRYP STUDY: SPECIFICITY OF SEROLOGICAL SCREENING TESTS FOR G-HAT IN IVORY COAST AND GUINEA

By Veerle Lejon

Serological screening plays a crucial role in the diagnosis of g-HAT, and seropositive cases are currently referred for microscopy testing. In the future, when a safe and easy-to-use drug becomes available, seropositive individuals could be treated immediately without the need for parasitological confirmation. This new case management strategy, known as Screen & Treat, will improve the detection and treatment of all HAT cases and, therefore, might end transmission faster.

Serological screening tests are based on antibody detection and can generate false positive results. As the Screen & Treat strategy aims to select individuals to be treated, the rate of false positives must be as low as possible to avoid treating people not infected with HAT. In compliance with the WHO's recent recommendation, the specificity of g-HAT screening tests should be at least 95%, or even higher. Over the past years, studies on the specificity of serological tests have produced variable results, and similar studies must be conducted on new RDTs and new experimental models. Furthermore, some HAT control programs have reported frequent cross-reactions with malaria infections, producing false positives for HAT screening.

The SpeSerTryp study was organised with the University Jean Lorougnon Guédé, Institut Pierre Richet, the National Programme for the Control of NTDs of Guinea, IRD, Institut Pasteur, CIRDES and FIND, to assess the specificity of HAT serological screening tests, alone and in conjunction with malaria status. Five serological tests were evaluated: three commercially available tests [CATT (ITM), Abbott Bioline HAT 2.0 (Abbott), HAT Sero-K-SeT (Coris Bioconcept)], and two investigational tests [DCN HAT RDT (DCN) and HAT Sero-K-SeT 2.0 (Coris Bioconcept)].

The study took place during an active screening campaign in HAT endemic areas in central Côte d'Ivoire and Guinea. Venous blood samples were taken from 1,095 participants and tested with the five HAT screening tests, along with a malaria RDT. Of these 1,095 individuals, 423 had at least one positive HAT screening test (seroprevalence 38.6%). All 423 samples were tested with mini column Anion Exchange Centrifugation Tube (mAECT) for parasitology and one HAT case was detected. The remaining 1,094 individuals were mAECT negative and considered HAT-free.

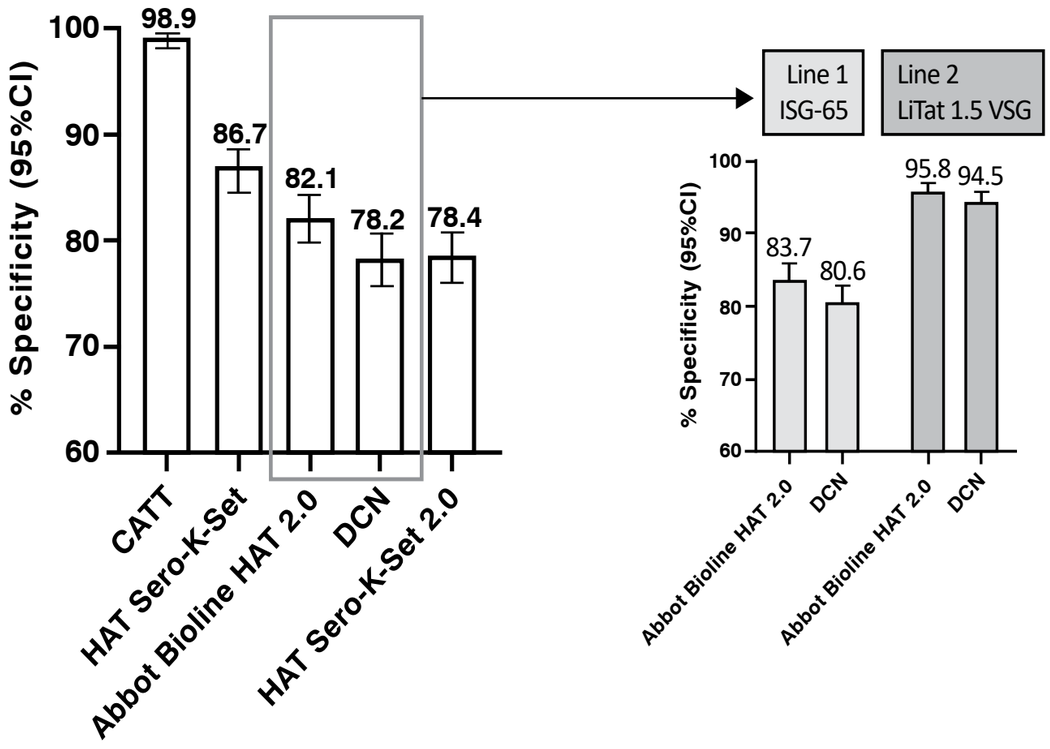
The CATT test had the highest specificity, at 98.9%. RDT specificity was surprisingly low (see Figure) with commercial kits (86.7% for HAT Sero-K-SeT and 82.1% for Abbott Bioline HAT 2.0 was 82.1%), as well as investigational kits (78.2% for DCN HAT RDT and 78.4% for HAT Sero-K-SeT 2.0). Abbott Bioline HAT 2.0 and DCN HAT RDTs have two separate test lines, and the specificity of the first test line was particularly low, respectively 83.7% and 80.6%, vs. 95% for the second test line. The overall malaria prevalence was 33.3%. The specificity of all HAT screening tests was slightly lower in the malaria positive group than in the malaria negative group, but the overall difference was not statistically significant.

This study shows that CATT specificity was higher than that of the RDTs, and thus CATT remains the test of choice for mass screening. For individual testing, RDTs are more practical but they generate many false positives and their specificity does not comply with the requirements

of a Screen & Treat strategy. The results of the individual test lines in Abbott Bioline HAT 2.0 and DCN HAT RDTs suggest that the first test line could be disregarded in favour of the second test line, but this approach is not ideal as it might reduce sensitivity and result in missing HAT cases. Combining both HAT Sero-K-SeT 2.0 and Abbott Bioline HAT 2.0 tests to improve specificity is an option currently implemented in Guinea.

Importantly, low specificity was observed not only in Côte d'Ivoire and Guinea, but also in a similar study carried out in the DRC. Research institutions and test manufacturers are actively collaborating to improve the performance of HAT RDTs.

Figure : 1



PARTICIPATION OF DNDI AND OTHER HAT PLATFORM PARTNERS IN THE 11TH EDCTP FORUM, 7-10 NOVEMBER 2023

By Florent Mbo and Olaf Valverde

DNDi and other HAT Platform partners actively participated in the 11th EDCTP Forum, whose theme was 'partnerships for innovation and impact in global health research'. We selected four abstracts on HAT, including two posters and two oral presentations. All presentations were published in the *British Medical Journal (Global Health)*.

1. *OA-504 Towards an arsenic-free oral treatment for human African trypanosomiasis due to Tb rhodesiense: a new tool for disease elimination.* *BMJ Global Health* Dec 2023, 8 (Suppl 10) A17; DOI: 10.1136/bmjgh-2023-EDC.39.

The primary efficacy endpoint of this clinical trial was reached, with no related deaths during hospitalisation (CI: 0.0-8.43%), compared with a past case fatality rate of 8.5% attributable to melarsoprol. Training was provided to health workers in twelve provinces in Uganda and three provinces in Malawi, which was more than expected. Two ethnographic studies providing up-to-date information on the perceptions of communities at risk of r-HAT led to four articles. Posters and brochures were produced and distributed in health facilities and at community gatherings.

The study showed that fexinidazole is a good alternative to existing treatments for oral treatment of both stages of r-HAT. It will be submitted for EMA regulatory review in preparation for use in endemic countries. Disease awareness has increased among health staff and populations living in endemic areas of Uganda and Malawi. In December 2023, EMA gave a postitive scientific opinion for fexinidazole as a new r-HAT treatment.

Authors: Olaf Valverde Mordt, Deolinda Alves, Jorge Seixas, Marshal Lemerani, Charles Wamboga, Elisabeth Baudin, Veerle Lejon, Aita Signorell, Enock Matovu.

1. *OA-765 Molecular diagnostic tests specificities and their contribution for HAT post-elimination monitoring in Burkina Faso and Côte d'Ivoire.* *BMJ Global Health* Dec 2023, 8 (Suppl 10) A22-A23; DOI: 10.1136/bmjgh-2023-EDC.52

The diagnostic specificity of all molecular tests (qPCR m18S, qPCR TgsGP and RIME LAMP) was high. A previous study demonstrated low analytical sensitivity for qPCR m18S and qPCR TgsGP (1,000 and 10,000 trypanosomes/mL, respectively), while parasitaemia recorded with the RIME LAMP (100 trypanosomes/mL) was within the range commonly observed in HAT patients. However, none of the three tests was entirely suitable for high-throughput use. The selection of the best algorithm for HAT post-elimination monitoring must take into account the cost of all possible algorithms, including of serological and parasitological diagnostics, based on the epidemiological context.

Authors: Charlie Franck Alfred Compaoré, Minayégninrin Koné, Jacques Kaboré, Hamidou Ilboudo, Mohamed Bamba, Hassane Sakande, Dramane Kaba, Adrien Marie Gaston Belem, Philippe Büscher, Veerle Lejon, Vincent Jamonneau

3. PA-80 Specificity of serological screening tests for diagnosis of gambiense human African trypanosomiasis in Côte d'Ivoire and Guinea. *BMJ Global Health* Dec 2023, 8 (Suppl 10) A32-A33; DOI: 10.1136/bmjgh-2023-EDC.78

The CATT test is more specific than RDTs for g-HAT diagnosis. The HAT Sero-K-SeT is more specific than second generation RDTs, which all contain the surface glycoprotein ISG-65, either as a separate test line (Bioline HAT 2.0 and DCN) or within a single mixed-antigen test line (HAT Sero-K-SeT 2.0). To improve specificity, removing ISG-65 from experimental RDTs, or ignoring the ISG-65 line, should be considered if this does not affect the test's sensitivity significantly.

Authors: Martial Kassi N'Djetchi, Oumou Camara, Mathurin Koffi, Mamadou Camara, Dramane Kaba, Traoré Barkissa Mélika, Minayégninrin Koné, Bamoro Coulibaly, Guy Pacôme Adingra, Aissata Soumah, Mohamed Diaby Gassama, Abdoulaye Dansy Camara, Bruno Bucheton, Vincent Jamonneau, Jean-Mathieu Bart, Sylvain Biéler, Veerle Lejon.

4. PA-580 Capacity development to facilitate delivery and uptake of a new medical intervention: fexinidazole oral treatment for the elimination of human African trypanosomiasis. *BMJ Global Health* Dec 2023, 8 (Suppl 10) A98; DOI: 10.1136

This project focused on capacity building and coordination support for the national healthcare systems of five countries (Angola, CAR, DRC, Guinea and South Sudan) for the appropriate use and surveillance of fexinidazole. It also contributed to the development of collaborative networking to extend pharmacovigilance activities to all drugs. Healthcare workers in all five countries were trained in the use of fexinidazole, and HAT patients are now being effectively diagnosed and treated.

Authors: Florent Mbo, Digas Ngolo, Eric Mwamba Miaka, Mamadou Camara, Albert Nyembo, Alphonsine Bilonda, Olaf Valverde Mordt

In addition to these presentations, DNDi also organised a round table entitled "Nothing less than health for all: essential elements for the control and sustainable elimination of Neglected Tropical Diseases (NTDs) through medical innovation". After an opening welcome and introduction by DNDi's Director General, Dr Luis Pizarro, four presentations were made by the following speakers:

1. Florent Mbo, Access Leader and HAT Platform Coordinator, DNDi: Innovative R&D and capacity building to eliminate sleeping sickness.

2. Fabiana Alves, NTD Leishmaniasis-Mycetoma Cluster Director: Visceral leishmaniasis on the cusp of a breakthrough with new therapeutic options.

3. Coralie Martin, Parasites and Free-Living Protists Team Leader, Muséum National d'Histoire Naturelle Paris: Helminths: partnerships for the pipeline.

4. Spring Gombe, Partner, Access to market in Africa, Germany: Nothing less than health for all – What is at stake when we talk about partnership and innovation for NTDs.

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VISITS AND MEETINGS

Joint exploratory visit to Angola by FIND, DNDi and LSTM partners on HAT control activities, 7-14 January 2023

Training of healthcare providers and members of the pharmacovigilance unit on electronic reporting, Forecariah, Guinea, 20-24 February 2023

Participation in the National Day on Human African Trypanosomiasis in the DRC, Kinshasa, DRC, 30 January 2023

WHO Programme for International Drug Monitoring (PIDM) in Africa, Rabat, Morocco, 26 February to 6 March 2023

Training of healthcare providers and members of the pharmacovigilance unit, Luanda, Angola, 10-17 February 2023

5th WHO stakeholder meeting on HAT elimination, Geneva, Switzerland, 7-9 June 2023

Participation in the StrogHAT project launch meeting, Antwerp, Belgium, 29-31 August 2023

Workshop to validate pharmacovigilance guidelines, Bangui, CAR, 10-12 October 2023

Training of healthcare providers and members of the pharmacovigilance unit in electronic reporting, Bangui, CAR, 8-16 October 2023

Training of laboratory technicians in sensitive diagnostic techniques, Bangui, CAR, 8-16 October 2023

Training of laboratory technicians in sensitive diagnostic techniques, Bangui, CAR, 8-16 October 2023

Participation in the EDCTP Forum in Paris, France, 7-10 November 2023

SCIENTIFIC PUBLICATIONS 2022/2023

1. Adugna Abera, Tihitina Mamecha, Ebise Abose et al. Reemergence of Human African Trypanosomiasis Caused by *Trypanosoma brucei rhodesiense*, Ethiopia. *Emerg Infect Dis*. 2024 Jan; 30(1):125-128. doi: 10.3201/eid3001.231319. Epub 2023 Nov 15

2. Kennedy PGE. The evolving spectrum of human African trypanosomiasis. QJM. 2024 Jun 25;117(6):391-395. doi: 10.1093/qjmed/hcad273. PMID: 38065835.

3. Philippe Solano, Fabrice Courtin, Dramane Kaba, Camara, Moïse Kagbadouno et al. Towards elimination of human African trypanosomiasis. *Med Trop Sante Int.* 2023 Feb 10;3 (1): mtsi. v3i1 .2023.317. doi: 10.48327/mtsi. v3i1.2023.317. eCollection 2023 Mar 31.

4. Tarral A, Hovsepian L, Duvauchelle T, Donazzolo Y, Latreille M, Felices M, Gualano V, Delhomme S, Valverde Mordt O, Blesson S, Voiriot P, Strub-Wourgaft N. Determination of the Optimal Single Dose Treatment for Acoziborole, a Novel Drug for the Treatment of Human African Trypanosomiasis: First-in-Human Study. *Clin Pharmacokinet*. 2023 Mar;62(3):481-491. doi: 10.1007/s40262-023-01216-8. Epub 2023 Feb 10.

5. Meisner J, Kato A, Lemerani MM, Miaka EM, Ismail AT, Wakefield J, Rowhani-Rahbar A, Pigott D, Mayer JD, Lorton C, Rabinowitz PM. Does a One Health approach to human African trypanosomiasis control hasten elimination? A stochastic compartmental modeling approach. *Acta Trop.* 2023 Apr: 240:106804. doi: 10.1016/j.actatropica.2022.106804. Epub 2023 Jan 19.

INTERNATIONAL MEETINGS 2024

1. 14-16 October 2024: 6th joint HAT Platform-EANETT scientific meeting, Conakry, Guinea.

2. 13-17 November 2024: 73rd annual meeting of ASTMH (American Society of Tropical Medicine and Hygiene), New Orleans Ernest N. Morial Convention Center, New Orleans, Louisiana, US

UPDATE ON DNDI'S FILARIASIS PROGRAMME

By Eric Kanza

View of a filariasis clinical trial site in the DRC

Onchocerciasis is a cutaneodermal filariasis caused by *Onchocerca Volvulus*, which is transmitted to humans by the bites of blackflies (genus Simulium). Ivermectin, currently approved for the treatment of onchocerciasis, is a microfilaricide. It eliminates microfilariae from the skin and temporarily prevents the adult female worm from releasing others.

Unfortunately, 6 to 8 months after treatment, the microfilariae return. A control strategy based on the distribution of ivermectin requires a long treatment period. To enable the effective elimination of onchocerciasis as a public health problem, we need to develop a macrofilaricidal drug (which kills the adult worm).

This is why DNDi, in partnership with PNLMTN-CTP, is simultaneously conducting two multicentre studies (flubentylosine-01 and Emodepside-04) on the development of a macrofilaricidal drug against onchocerciasis.

1. Flubentylosine-01 study

Flubentylosine (previsously known as TylAMac or ABBV-4083) is a macrolide antibiotic used in animal health.antibiotic used in animal health.

Study title:
A phase II, randomised, double-blind, parallel-group study evaluating emodepside (BAY 44-4400) in patients with *Onchocerca volvulus* infection, including *Onchocerca volvulus* infection, comprising :

- Part 1, assessing safety, tolerability,efficacy for dose determination and pharmacokinetics
- Parti 2, assessing the efficacy of selected doses safety, tolerability and pharmacokinetics.

The objective of part 1 of this study was to determine whether treatment with flubentylosine or with flubentylosine + albendazole resulted in effective depletion of *Wolbachia* bacteria in adult female female worms at 6 months on the basis of immunohistology of the onchocercian nodules. For this study, 153 participants were randomized and 151 were treated. However, 149 completed the study. The results will be shared at a later date.

2. Emodepside study

Emodepside is also an anthelmintic used in animal health.

Study title :
A double-blind, randomised, parallel-group, phase II study evaluating emodepside (BAY 44-4400) in patients with *Onchocerca volvulus* infection, including:

- Part 1 evaluating safety, tolerability, pharmacodynamics, pharmacokinetics and dose-response dose-response relationship for efficacy (proof of concept)
- Part 2 assessing the efficacy of selected doses, safety, tolerability and pharmacokinetics

The objective of part 1 of the development of this study is to determine whether emodepside will sterilise adult female worms and/or have a macrofilaricidal effect at 12 months.

Inclusion in this study has already been completed. 158 subjects have been randomised in this study, follow-up visits are finished and the last visit of the last participant took place before the end of March 2024.

Courses of study

- These studies are being carried out at two sites, Masi-Manimba General Referral Hospital and Kimpese referral health centre.
- They are conducted in accordance with European standards with:
  - Qualified and experienced staff trained in the good clinical practices of the International Conference on Harmonisation (ICH);
  - State-of-the-art laboratory and ophthalmology laboratory and ophthalmology equipment to monitor study participants.
- Appropriate accommodation for participants.

Difficulties encountered
Onchocerciasis being a disease of the 'end of the road', we have to contend mainly with the poor state of the roads, especially in the rainy season, in order to reach the villages where study participants are recruited.

Visit of filariasis clinical trial site in the DRC by DNDI Executive Director, Dr Luis Pizarro

UPDATE ON DNDI'S PAEDIATRIC HIV PROGRAMME

By Aimé Mboyo, Jean Louis Bobozo, Michel Diyi, Filmon Abraha, Justine and Florent Mbo

Visit of treatment site by the head of HIV DNDI

Access to prevention, care and treatment for children under the age of 15 remains a challenge in the DRC. Coverage of HIV-positive children on antiretroviral treatment (ART) rose from 23% in 2015 to 33.2% in 2019, but there are major disparities between the different provinces affected. A number of factors are at the root of these disparities: poor access to diagnosis and to optimal antiretrovirals (ARV), lack of training for healthcare providers and lack of awareness-raising at community level.

The aim of the project implemented by DNDi in the North and South Ubangi provinces of the DRC (an area in which there are virtually no basic HIV services) is to provide immediate access to optimal treatment for children under the age of 3. The first-line treatment in the DRC is pDTG (paediatric dolutegravir), while the combination of abacavir (ABC), lamivudine (3TC), lopinavir and ritonavir (LPV/r) called '4-in-1' is an alternative treatment. Started in December 2022, this treatment access programme implemented by the PNLS (National AIDS Control Programme), of which DNDi is the promoter, has made it possible to: 1) test 8,530 women, of whom 65 women have been diagnosed HIV+; 2) examine 107 children and treat 25 infected children; 3) organise the training of 84 healthcare providers (doctors and nurses) as well as 42 laboratory technicians and 126 community workers.

Preliminary results:

1. 9 months after the launch of this access project (in September 2023), 21 children were started on oral granules of '4-in-1', and 7 had their viral load suppressed at the follow-up visit. Vomiting was observed. The weights of these 7 children, although low, varied between 5 and 8 kg, while their ages ranged from 3 months to 19 months. The technique used to measure viral load was GeneXpert. Of the 7 children, 5 had a viral load of less than 40 copies/ml, while two children had viral loads of 103 and 88 copies/ml respectively.

2. With regard to the objectives 95% 95% 95% by 2030, we believe that this project meets these objectives, as it has enabled HIV control activities to be implemented in a virgin area. All the children and women who tested positive for HIV received treatment.

3. A transition plan for activities with the PNLS is underway and will enable the PNLS to include this cohort of children with HIV under '4-in-1' in the country's overall plan, with the use of paediatric dolutegravir.

Note: 95%95%95% by 2030 targets: With its country partners, UNAIDS has set a global target global target for 2030: 95-95-95, i.e. to diagnose 95% of all people living with HIV, provide ARV treatment to 95% of those diagnosed, and to get an undetectable viral load in 95% of those treated, by 2030

Treatment and DNDI site team

OBITUARIES

Tribute to the late Bakomeka Mpeya, Provincial Supervisor of the NSSCP in the DRC

By Dr Pathou Nganzobo

Bakomeka Mpeya, affectionately known as Papa Super or Super Bako, was one of the DRC's most experienced NSSCP supervisors. He was the Provincial Supervisor of the Bandundu Nord Coordination Centre, a reliable and assiduous collaborator, and an advisor on technical matters. No decision was taken without his advice, which was always relevant. He worked tirelessly with the mobile teams, particularly in planning active screening for sleeping sickness in endemic villages, and he provided guidance to the research teams in the field. He was also a major contributor to the supervision of the new provincial coordinating doctors sent by the national centre for training at the NSSCP Bandundu Nord Coordination Centre. He was in the habit of saying that "You only recognise the importance of people when they leave".

With these words, we would like to thank his family for the work he did for the Congolese nation in general, and for the fight against sleeping sickness in particular, in the Bandundu Nord Coordination. We have lost a manager, an advisor, a colleague and a big brother whose way of life was commendable.

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BIRTHS

Grâce Ndeji Ntambue, born on August, 18th, 2023, daughter of Laurent Ciebue, lab assistant DNDi, DRC

Mel Kavunga Dinanga, born on September, 21th, 2023, son of Papy Kavunga, DNDI monitor, DNDi, DRC

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- Medicor Foundation
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- Spanish Agency for International Development Cooperation (AECID), Spain
- Swiss Agency for Development and Cooperation (SDC), Switzerland
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